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EXAMINER	
POLANSKY, GREGG	
ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/522,035	CHARBIT ET AL.	
	Examiner	Art Unit	
	GREGG POLANSKY	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 October 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5 and 11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-5 and 11* is/are rejected.

7)☒ Claim(s) *1* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 October 2008* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Applicants' response, filed 10/03/2008, to the Office Action mailed 7/03/2008 is acknowledged. Applicants canceled Claim 2, amended Claims 1 and 3, and presented arguments in response to the Office Action.

2. Claims 1, 3-5, and 11 are pending and presently under consideration.

3. Applicants' arguments have been fully considered and are persuasive in part. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Objections

4. Claim 1 is objected to because of the following informalities: The 2nd line of Claim 1 recites "transplant rejection by increasing the levels of **a-heme** oxygenase enzyme in a" (emphasis added). This appears to be a typographical error. Appropriate correction is required.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1 and 3-5 remain rejected under 35 U.S.C. 102(b) as being anticipated by Moore et al. (Osteoarthritis and Cartilage, Vol. 6, pages 19-23).

Moore et al. teach diacerhein inhibits granuloma induced cartilage breakdown in rat femoral cartilage subcutaneously implanted (i.e., transplanted) in mice. The doses of diacerhein administered to the mice were 5, 15, or 50 mg/kg, administered orally. See "Summary", page 19 and last paragraph, page 23.

Moore et al. do not teach rhein or rhein derivatives increasing the levels of a heme oxygenase enzyme. However, it is noted that *In re Best* (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter, which there is reason to believe inherently includes functions that are newly cited, or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter to be shown in the prior art does not possess the characteristic relied on" (205 USPQ 594, second column, first full paragraph). In the instant invention, the applicants must show that the teachings of Moore et al. do not work through the instant invention mechanism of up-regulation of a heme oxygenase enzyme. There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. *Schering Corp. v. Geneva Pharm. Inc.*, 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003); see also *Toro Co. v. Deere & Co.*, 355 F.3d 1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004) ("[T]he fact that a characteristic is a necessary feature or result of a prior-art

embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention").

As required by instant claim 4, the determination of optimal dosage ranges is well within the purview of those skilled in the art through no more than routine experimentation. It is not inventive to discover the optimum or workable ranges by routine experimentation when general conditions of a claim are disclosed in the prior art. See *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233,235 (CCPA 1955) and MPEP 2144.05(11).

Applicants' argue "Moore is directed to osteoarthritis, which is not related to treatment of transplant rejection. Moore also fails to disclose any increase in heme oxygenase enzyme levels and certainly fails to disclose that such an increase could treat transplant rejection".

This argument is not persuasive. As presented *supra*, Moore et al. teach diacerhein inhibits granuloma induced cartilage breakdown in rat femoral cartilage subcutaneously implanted (i.e., transplanted) in mice. Thus, Moore et al. teach the use of diacerhein in the treatment of transplant (i.e., rat femoral cartilage) rejection. See *In re Best* discussion, above, with regard to increasing levels of a heme oxygenase by diacerhein.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1, 3-5, and 11 remain rejected under 35 U.S.C. 103(a) over Charbit et al. (U.S. Patent No. 6610750), in view of in view of Häyry (Abstract).

Charbit et al. teach a method of treating osteoarthritis, an inflammatory disease or condition, or an autoimmune disease, by the administration of diacerein, rhein and derivatives of rhein, at a dose of 25-500 mg/day (*see* column 7, 3rd paragraph, and claims 1, 3-5). Oral administration of unitary doses of between 20 and 50 mg of diacerein is disclosed in column 6, lines 34-41.

Häyry teaches that "the etiology of chronic [allograft] rejection is most probably multifactorial" and that "the common feature in all organ allografts undergoing chronic rejections is persistent perivascular inflammation…".

One of ordinary skill has good reason to pursue the known options within his or her technical grasp. Therefore it would have been obvious to try to treat organ rejection

by taking advantage of the anti-inflammatory properties of diacerein. Seeking a method of treating transplant rejection would have been further motivation to combine the teachings of Charbit et al. and Häyry.

Charbit et al. do not teach rhein or rhein derivatives increasing the levels of a heme oxygenase enzyme. However, it is noted that *In re Best* (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter, which there is reason to believe inherently includes functions that are newly cited, or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter to be shown in the prior art does not possess the characteristic relied on" (205 USPQ 594, second column, first full paragraph). In the instant invention, the applicants must show that the teachings of Charbit et al. (i.e., treating osteoarthritis, inflammatory diseases/conditions or autoimmune diseases with rhein or diacerein) do not work through the instant invention mechanism of up-regulation of a heme oxygenase enzyme. There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. *Schering Corp. v. Geneva Pharm. Inc.*, 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003); see also *Toro Co. v. Deere & Co.*, 355 F.3d 1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004) ("[T]he fact that a characteristic is a necessary feature or result of a prior-art embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention").

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole is *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicants argue "Charbit discloses the treatment of osteoarthritis, by delaying the progression of the destruction of the joint cartilage. However, Charbit does not disclose the use of diacerein in the treatment of transplant rejection by increasing levels of the heme oxygenase enzyme. Häyry fails to remedy these deficiencies."

This argument is not persuasive. As presented *supra*, Charbit et al. teach a method of treating osteoarthritis, an inflammatory disease or condition, or an autoimmune disease, by the administration of diacerein, rhein and derivatives of rhein. Häyry teaches that "the etiology of chronic [allograft] rejection is most probably multifactorial" and that "the common feature in all organ allografts undergoing chronic rejections is persistent perivascular inflammation…". One of ordinary skill has good reason to pursue the known options within his or her technical grasp. Therefore it would have been obvious to try to treat organ rejection by taking advantage of the anti-

inflammatory properties of diacerein. See *In re Best* discussion, above, with regard to increasing levels of a heme oxygenase by diacerhein.

10. Claims 1, 3-5 and 11 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Moore et al. (Osteoarthritis and Cartilage, Vol. 6, pages 19-23) (provided by Applicants), in view of Charbit et al. (U.S. Patent No. 6610750).

The teachings of Moore et al. and Charbit et al. are presented *supra*.

Moore et al. does not teach the unitary doses required by instant Claim 11. As presented *supra*, Charbit et al. teach unitary doses of between 20 and 50 mg of diacerein.

It would have been obvious to one of ordinary skill at the time of the invention to utilize the unitary doses taught by Charbit et al. in combination with the teachings of Moore et al. One would have been motivated to treat transplant rejection with diacerhein as taught by Moore et al. and suggested by Charbit et al., with the unitary doses taught by Charbit et al. Because both references teach the oral administration of diacerhein for the treatment of conditions which read on the instantly claimed invention.

Applicants reiterate their arguments to art of the previous rejections. These arguments have been addressed *supra*.

Conclusion

11. Claims 1, 3-5 and 11 are rejected.

12. No claims are allowed.

13. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to GREGG POLANSKY whose telephone number is (571)272-9070. The examiner can normally be reached on Mon-Thur 9:30 A.M. - 7:00 P.M. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Gregg Polansky/
Examiner, Art Unit 1614

/Ardin Marschel/

Supervisory Patent Examiner, Art Unit 1614